REMARKS

The Office Action of August 9, 2005 presents the examination of claims 1-3 and 5-8.

Rejection for lack of enablement

Claims 1-3 and 5-8 are rejected under 35 USC § 112, first paragraph, for alleged lack of enabling disclosure in the specification. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner acknowledges that the invention is operable using 40 ng of input genomic DNA per 100 sites. However, he disputes operability of the invention at the lower limit of 10 ng per 100 sites that is recited in claim 1.

Applicants submit that the Examiner must accept statements made in the specification as true, absent objective evidence or sound scientifically derived reasons to the contrary. *In re Marzocchi and Horton*, 169 USPQ 367 (CCPA 1971). In the present instance, the Examiner fails to provide such objective evidence or sound scientifically derived reasons.

The Examiner acknowledges that the working example from the specification establishes operability of the invention at the level of 40 ng of input genomic DNA per 100 SNP sites, but argues that due to unpredictability in the art and lack of an actual demonstration of operability, it is not established that the claimed assay is operable at only 10 ng of input genomic DNA per 100 SNP sites. The Examiner points to Mein et al. (Genome Research 2000) as stating that [2-3]% of the assays attempted failed due to PCR failure. The Examiner reads Mein rather selectively, ignoring that Mein describes development of an assay for a number of specific SNP sites and that initial PCR failures were typically later cured by redesign of one or more of the primers utilized. (See the last paragraph at page 340, first column). Also, the "underlying rate of PCR failure" includes at least some component of operator error, rather than a systemic failure of the specific assay. ("Ninety-two percent of the initial mistypings with the PCR-Invader assay are assumed to be a failure to deliver template to the one of the reactions...").

The Examiner also cites the rather low success rate of only 50% of Wang et al. (Science 1998) when using more DNA in a very highly multiplexed assay. Wang et al. utilize hybridization of the PCR product to SNP-specific sites on a solid phase "chip" for detection, not an Invader or Taq-Man assay, and so the results of Wang et al. are somewhat irrelevant to predictability of the operability of the present invention.

For the above reasons, Applicants submit that the Examiner fails to establish any good reason to doubt Applicants' statements in the specification to the effect that the instant invention is operable as claimed and the rejection of claims 1-3 and 5-8 under 35 USC § 112, first paragraph, for lack of enablement by the specification, should be withdrawn.

"New matter" rejection

Claims 1-3 and 5-8 are rejected under 35 USC § 112, first paragraph, for alleged lack of written decription support in the specification. The Examiner asserts that the success rate for the claimed assay in detecting at least 98% of SNPs assayed at the level of input DNA of other than 40 ng is "new matter".

The legal test for adequacy of written description is whether one of ordinary skill in the art who reads the specification would understand the inventors to be in "possession" of the invention as claimed. Applicants submit that the specification expressly states this detection level at 40 ng input DNA in a working example. As explained above, the Examiner has failed to demonstrate sufficiently any reason to doubt that the 98% or greater detection efficiency of the described method should be less when an amount of input DNA other than 40 ng input DNA is used. The Examiner merely states the legal test for adequate written description and a conclusion that it is not met, without explaining why one of ordinary skill in the art who reads the working example would not understand the results obtained using 40 ng of input DNA are not applicable to other amounts of input DNA.

Accordingly, the Examiner has not met his burden of establishing a lack of adequacy of the written description of the specification and the instant rejection should be withdrawn.

Rejections over prior art

Claims 1 and 5 are rejected under 35 USC § 102(b) as anticipated by Mein et al. (Science 2000). This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Both claims 1 and 5 are directed to a multiplexed assay and recite that a plurality of nucleotide sequences are amplified simultaneously. Mein et al. do not describe or suggest this. The Examiner should note, e.g. that Table 1 in Mein shows that the different Invader primers are designed with distinct annealing temperatures, precluding a multiplex assay. The Examiner might further note that the experimental section of Mein, under "PCR" describes that the PCR conditions were optimized for each amplification primer set by varying Mg concentrations and annealing temperatures. Thus, it is plain that Mein et al. perform amplification of only one nucleotide sequence at a time. Accordingly, the instant rejection should be withdrawn.

Claims 3 and 7 stand rejected under 35 USC § 103(a) as being unpatentable over Mein et al. in view of Wang. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

The Examiner asserts that Mein et al. describe a multiplex amplification of polymorphic loci. However, this is not the case. It is true that Mein et al. describe genotyping of a plurality of loci, but the assays are run in a serial, not a multiplexed, fashion. Thus, Mein utilizes 10 ng of input DNA per single SNP site (or in the five instances described of one PCR product encompassing multiple loci, perhaps 10 ng per two or three sites).

Wang et al. do describe a multiplex assay, but encounter a high failure rate, especially when using the low level of input DNA of 10-40 ng per 100 SNP sites. Thus, Wang et al. actually teach away from the present invention, as was explained in Applicants' previous paper.

The Examiner asserts that overcoming the high failure rate encountered by Wang is a mere optimization problem. However, Applicants submit that this is inconsistent with the presentation of a rejection for lack of enablement based upon unpredictability in the art.

The Examiner fails to establish prima facie obviousness of the invention in view of the combination of Mein with Wang. The Examiner inappropriately combines Mein with Wang as Wang teaches away from the instant invention. Furthermore, even it the combination of these references is deemed appropriate, the combined references at best describe a multiplex PCR that produces a failure rate of 50% when as little as 10-40 ng of input genomic DNA are utilized. This combination does not include every feature of the invention as claimed.

As the Examiner fails to establish prima facie obviousness of the invention, the instant rejection of claims 3 and 7 under 103(a) over Mein in view of Wang should be withdrawn.

Claims 2 and 6 are rejected under 35 USC § 103(a) as being unpatentable over Mein et al. in view of Brookes '670. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Again, the Examiner fails to establish prima facie obviousness of the invention as claimed. The deficiencies of Mein in describing at least one basic aspect of the instant invention are explained above. Brooks is cited for the "hot start" feature recited in claims 2 and 6. Brookes also does not describe a multiplex assay in which a plurality of polynucleotide sequences is simultaneously amplified. Thus, the combination of Mein with Brookes fails to establish prima facie obviousness of the invention recited in claims 2 and 6. Accordingly the instant rejection should be withdrawn.

Claim 8 is rejected under 35 USC § 103(a) as being unpatentable over Mein in view of Wang and Brookes. This rejection is respectfully traversed. Reconsideration and withdrawal thereof are requested.

Claim 8 recites using both "hot start" PCR and that at least 50 sets of primers are used in the simultaneous PCR amplification step. As explained above, the combination of Mein and Wang fails to describe a multiplex assay in which at least 98% of the SNPs are detected. Although describing hot start PCR, Brookes does not remedy the deficiencies of Mein and Wang in describing the invention as recited in claim 8 for the reasons set forth above.

The combined references fail to describe or suggest each and every feature of claim 8, and accordingly the Examiner fails to establish prima facie obviousness of the invention. Thus the instant rejection should be withdrawn.

The present application well-describes and claims patentable subject matter. The favorable action of allowance of the pending claims and passage of the application to issue is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell (Reg. No. 36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

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Respectfully submitted,

By _____

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